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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/436,347	11/09/1999	CHRISTINE A. WHITE	27693-01201	6491

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SIDLEY AUSTIN LLP
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EXAMINER	
HARRIS, ALANA M	

ART UNIT	PAPER NUMBER
1643	

DATE MAILED: 10/27/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/436,347	WHITE ET AL.	
	Examiner	Art Unit	
	Alana M. Harris, Ph.D.	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 August 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *29-94* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *29-94* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Request for Continued Examination

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on August 7, 2006 has been entered.

2. Claims 29-94 are pending.

Claims 4-11, 13, 14 and 16-18 have been cancelled.

Claims 29-94 are examined on the merits.

Withdrawn Grounds of Rejection

Claim Rejections - 35 USC § 102

3. The rejection of claims 4, 5, 8, 11, 13, 14, 16 and 28 under 35 U.S.C. 102(e) as being anticipated by U.S. Patent number 6,090,365 (field November 18, 1997) is withdrawn in light of the cancellation of the claims.

Claim Rejections - 35 USC § 103

4. The rejection of claims 4, 5, 8, 11, 13, 14, 16 and 28 under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent number 6,090,365 (field November 18, 1997), in

view of McLaughlin et al. (Journal of Clinical Oncology 16(8): 2825-2833, August 1998/ IDS reference B1, submitted October 19, 2004), U.S. Patent number 6,682,734 (effective filing date November 13, 1992) and EP document 0 510 949 A2 (April 23, 1991) is withdrawn in light of the cancellation of the claims.

New Grounds of Objection

Claim Objections

5. Claims 41, 67 and 89 are objected to because of the following informalities: they recite different spellings, fludarabine and fludaribine. Applicants should recite the proper spelling of the drug, which is fludarabine and cite consistent language in the claims.

Claim 92 is objected to because of the following informality: "toremifine" should be spelled "toremifene". Applicants should recite the proper spelling of the drug and review the entire specification for similar errors.

New Grounds of Rejections

Claim Rejections - 35 USC § 112

6. Claims 29-94 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **THIS IS A NEW MATTER REJECTION.**

Applicants have introduced new claims to include the recitation "...administering an unlabeled anti-CD20 antibody to the patient...to treat the chronic lymphocytic leukemia." Via voice mail left for the Examiner by David Fitzgerald on October 11, 2006 he asserts support for the recitation is found in the specification in section 0330 on page 9. The Examiner has reviewed this section of the specification and does not concur. This paragraph reads on unlabeled immunoglobulins may be useful in the treatment of non-Hodgkin's lymphoma. While this disease is a hematologic malignancy, such as chronic lymphocytic leukemia (CLL) the passage is not sufficient to provide support to Applicants' claims reading on treating CLL with an unlabeled anti-CD20. The two diseases are not one and the same. Applicants should delete the new matter or explicitly point out by page and section number where support may be found for this new limitation.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

8. The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting

directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

9. Claims 29-32, 42, 44, 46, 53-58, 68, 70-72, 79-88, 90 and 91 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent number 6,090,365 (filed November 18, 1997). In anticipation of the instant rejection Applicants assert "the patent arguably suggests the applicants' desire to include treatments of CLL" and "there is in fact no description and no exemplification of a specific treatment of any CLL patient using any anti-CD20 antibody", see Remarks submitted August 7, 2006, page 16, 2nd paragraph. Applicants direct the Examiner's attention to several passages allegedly teaching away or not enabling the method of the claimed invention. These points of view have been carefully reviewed and considered, but found unpersuasive.

Applicants' are reminded that the claims include open language, comprising and treating according to the claims reads plainly on administering an unlabeled anti-CD20 antibody to a patient in order to treat CLL. Treating is broadly interpreted as giving medical aid to counteract a disease or condition. The specification does not contain a definition limiting the scope of "treating". Consequently, the patent is anticipatory disclosing methods for treatment of chronic lymphocytic leukemia (CLL), chronic myeloblastic leukemia and lymphomas by administration of a B-cell specific antibody, unlabeled antibody B1, see the abstract; column 5, lines 25-35; column 7, lines 24-47; and column 13, lines 40-61. Unlabeled B1 was administered intravenously, see column 29, lines 47-56. The disclosed method sets forth the concurrent treatments of

an antibody or antibody fragment that binds to the CD20 antigen and the administration of a radioisotope conjugated to said antibodies or a chemotherapeutic agent, such as chlorambucil and oncovin, also known as vincristine see column 35, lines 12-20; column 38, claim 11 and column 39, claim 14.

The patent discloses the use of antibodies comprising the B1 antigen-binding domain, as well as alternative method of "humanization "of the antibody and Fab, Fab', or $F(ab')_2$ fragments administered in a range from 0.2 to 40 mg/kg, which reads on Applicants' range, see column 7, line 57- column 8, line 11 and column 10, lines 62-64.

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. Claims 29-94 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent number 6,090,365 (filed November 18, 1997), and further in view of McLaughlin et al. (Journal of Clinical Oncology 16(8): 2825-2833, August 1998/ IDS reference B1, submitted October 19, 2004), Stenbygaard et al. (Breast Cancer Research and Treatment 25: 57-63, 1993) and U.S. Patent number 6,399,649 B1 (effective filing date September 24, 1998). The teachings of U.S. patent #6,090,365 were presented in the 102(e) rejection. The patent does not teach the claimed method,

wherein the antibody is explicitly rituximab, weekly for about 2 to 10 weeks, at a dosage of a 375mg/m^2 weekly for a total of four weeks, particularly administered at an initial dose of 100mg/m^2 and the remainder of a 375mg/m^2 is administered on the following day and the other particular time points and dosages. Patent '365 also does not teach the method the execution of the method in a patient previously treated for CLL and treated with fludaribine, toremifene and tamoxifen and was refractory to fludaribine.

However, McLaughlin teaches a method of treating patients with several types of lymphoma with the administration of a chimeric anti-CD20 monoclonal antibody, rituximab (IDEC-C2B8), see title and Patients and Methods section on page 2826, column 1. All of the patients were given an antibody dose of 375mg/m^2 intravenously once weekly for a total of four infusions, see abstract and page 2826, column 1, Therapy section. Patients had to have either not responded to primary therapy or relapsed in order to participate in the study, see page 2826, 1st column, Eligibility section. "The initial infusion rate was 50mg/h, with subsequent infusion rate increase...", see cited Therapy section.

U.S. patent #6,399,649 teaches alternative approaches to CLL treatment after failed attempts of fludarabine administration because of a refractory response, see column 1, lines 46-56. And Stenbygaard teaches the implementation of chemotherapeutic agents, toremifene and tamoxifen in the treatment of cancer.

Additionally, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to administer the anti-CD20 antibody in the recited dosages. One of ordinary skill in the art would have been motivated to do so

with a reasonable expectation of success by teachings well known in the art, that dosages of any pharmaceutical composition must be adjusted and optimized.

It would have been *prima facie* to one of ordinary skill in the art at the time the claimed invention was made to combine the teachings of McLaughlin and both patents to efficaciously treat cancer. One of ordinary skill in the art would have been motivated to combine the teachings of all the documents because McLaughlin cites there has been "...evidence of synergism between [rituxumab] and some chemotherapeutic agents" to implement targeted immunotherapy and consequently specifically destroy cells associated with a pathogenic condition (i.e. leukemias and lymphomas), see McLaughlin page 2831, column 2, last paragraph; the patent, column 3, lines 55-58 and column 8, line 11-column 9, line 22; and entire Stenbygaard article.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alana M. Harris, Ph.D. whose telephone number is (571)272-0831. The Examiner works a flexible schedule, however she can normally be reached between the hours of 7:30 am to 6:30 pm with alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry R. Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

ALANA M. HARRIS, PH.D.
PRIMARY EXAMINER

Alana M. Harris, Ph.D.
16 October 2006